CLAIMS

1. A method of screening a compound or its salt that alters the binding property or signal transduction between (1) a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or a salt thereof and (2) humanin or a salt thereof, which comprises using the receptor protein, a partial peptide thereof or a salt thereof and humanin or a salt thereof.

2. The screening method according to claim 1, wherein the humanin is:

(1) a polypeptide comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 3 or a salt thereof,

(2) a peptide consisting of consecutive 6 to 20 amino acids in the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 3 or a salt thereof, or

(3) a polypeptide comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 7 or a salt thereof.

3. The screening method according to claim 1, wherein the humanin is:

(1) a polypeptide or its salt consisting of a) the amino acid sequence represented by SEQ ID NO: 3, b) an amino acid sequence represented by SEQ ID NO: 3 wherein 1 to 10 amino acids are deleted, c) an amino acid sequence represented by SEQ ID NO: 3 to which 1 to 10 amino acids are added, d) an amino acid sequence represented by SEQ ID NO: 3 wherein 1 to 5 amino acids are substituted by other amino acids, or e) an amino acid sequence consisting of the above amino acid sequence with a combination of deletion, addition and substitution mentioned above,

(2) a polypeptide or its salt consisting of a) the amino acid sequence represented by SEQ ID NO: 4, b) an amino acid sequence represented by SEQ ID NO: 4 wherein 1 to 10 amino acids are deleted, c) an amino acid sequence represented by SEQ ID NO: 4 to which 1 to 10 amino acids are added, d) an amino acid sequence represented by SEQ ID NO: 4 wherein 1 to 5 amino acids are substituted by other amino acids, or e) an amino acid sequence consisting of the above amino acid sequence with a combination of deletion, addition and substitution mentioned above,

(3) a polypeptide or its salt consisting of a) the amino acid sequence represented by SEQ ID NO: 8, b) an amino acid sequence represented by SEQ ID NO: 8 wherein 1 to 10 amino acids are deleted, c) an amino acid sequence represented by SEQ ID NO: 8 to which 1 to 10 amino acids are added, d) an amino acid sequence represented by SEQ ID NO: 8 wherein 1 to 5 amino acids are substituted by other amino acids, or e) an amino acid sequence consisting of the above amino acid sequence with a combination of deletion, addition and substitution mentioned above,

(4) a peptide wherein the number of amino acids is 6 to 20, or its salt, consisting of a) an amino acid sequence in positions 19 to 24, positions 5 to 24, positions 1 to 20, positions 5 to 20 or positions 5 to 21 in the amino acid sequence represented by SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 8, b) an amino acid sequence comprising the above amino acid sequence wherein 1 to 6 amino acids are deleted, c) an amino acid sequence comprising the above amino acid sequence wherein 1 to 6 amino acids are added, d) an amino acid sequence comprising the above amino acid sequence wherein 1 to 6 amino acids are substituted by other amino acids, and e) an amino acid sequence comprising the above amino acid sequence with a combination of deletion, addition and substitution mentioned above, provided that the peptide does not include a peptide consisting of an amino acid sequence in positions 19 to 24, positions 5 to 24, positions 1 to 20, positions 5 to 20 or positions 5 to 21 in the amino acid sequence represented by SEQ ID NO: 5, or

(5) a polypeptide or its salt consisting of a) the amino acid sequence represented by SEQ ID NO: 7, b) an amino acid sequence represented by SEQ ID NO: 7 wherein 1 to 10 amino acids are deleted, c) an amino acid sequence represented by SEQ ID NO: 7 to which 1 to 10 amino acids are added, d) an amino acid sequence represented by SEQ ID NO: 7 wherein 1 to 10 amino acids are substituted by other amino acids, or e) an amino acid sequence consisting of the above amino acid sequence with a combination of deletion, addition and substitution mentioned above.

4. The screening method according to claim 1, wherein the humanin is:

(1) a polypeptide consisting of the amino acid sequence represented by SEQ ID NO: 3 or a salt thereof,

(2) a polypeptide consisting of the amino acid sequence represented by SEQ ID NO: 4 or a salt thereof,

(3) a polypeptide consisting of the amino acid sequence represented by SEQ ID

NO: 6 or a salt thereof,

(4) a polypeptide consisting of the amino acid sequence represented by SEQ ID NO: 7 or a salt thereof,

(5) a polypeptide consisting of the amino acid sequence represented by SEQ ID NO: 8 or a salt thereof,

(6) a polypeptide consisting of the amino acid sequence represented by SEQ ID NO: 9 or a salt thereof, or

(7) a peptide or its salt consisting of a) an amino acid sequence in positions 19 to 24, positions 5 to 24, positions 1 to 20, positions 5 to 20 or positions 5 to 21 in the amino acid sequence represented by SEQ ID NO: 3, SEQ ID NO: 4 or SEQ ID NO: 8.

5. The screening method according to claim 1, wherein the amino group of an N-terminus methionine residue of humanin is formylated.

6. The screening method according to claim 1, wherein the humanin is a polypeptide, or its salt, consisting of the amino acid sequence represented by SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8 or SEQ ID NO: 9, wherein the amino group of an N-terminal methionine residue thereof is formylated.

7. A kit for screening a compound or its salt that alters the binding property or signal transduction between (1) a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or a salt thereof and (2) humanin or a salt thereof, which comprises the receptor protein, a partial peptide thereof or a salt thereof and humanin or a salt thereof.

8. A compound or its salt that alters the binding property or signal transduction between humanin or a salt thereof and a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or a salt thereof, which is obtainable using the screening method according to claim 1 or the screening kit according to claim 7.

9. The compound according to claim 8, wherein the compound is an agonist.

10. The compound according to claim 8, wherein the compound is an antagonist.

11. A pharmaceutical preparation comprising a compound or its salt that alters the binding property or signal transduction between humanin or a salt thereof and a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or a salt thereof.

12. A prophylactic/therapeutic agent for nerve degeneration diseases or brain function disorders, which comprises an agonist to a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or to a salt thereof.

13. The prophylactic/therapeutic agent according to claim 12, which is a prophylactic/therapeutic agent for Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral disease, epidural hematoma or subdural hematoma.

14. An apotosis inhibitor comprising an agonist to a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or to a salt thereof.

15. A prophylactic/therapeutic agent for nerve degeneration diseases or brain function disorders, which comprises a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10 or SEQ ID NO: 14, or a partial salt thereof or a salt thereof.

16. The prophylactic/therapeutic agent according to claim 15, which is a prophylactic/therapeutic agent for Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral disease, epidural hematoma or subdural hematoma.

17. An apotosis inhibitor comprising a G protein-coupled receptor protein

comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, or a partial peptide thereof or a salt thereof.

18. A prophylactic/therapeutic agent for nerve degeneration diseases or brain function disorders, which comprises a polynucleotide comprising a polynucleotide encoding a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, or a partial peptide thereof.

19. The prophylactic/therapeutic agent according to claim 18, which is a prophylactic/therapeutic agent for Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral disease, epidural hematoma or subdural hematoma.

20. An apotosis inhibitor comprising a polynucleotide comprising a polynucleotide encoding a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, or a partial peptide thereof.

21. A diagnostic agent for diseases involving nerve degeneration, which comprises a polynucleotide comprising a polynucleotide encoding a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or a partial peptide thereof.

22. The diagnostic agent according to claim 21, which is a diagnostic agent for Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral disease, epidural hematoma or subdural hematoma.

23. A diagnostic agent for diseases involving nerve degeneration, which comprises an antibody to a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1,

SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, or to a partial peptide thereof or to a salt thereof.

24. The diagnostic agent according to claim 23, which is a diagnostic agent for Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral disease, epidural hematoma or subdural hematoma.

25. A method of screening a compound or its salt preventing and treating nerve degeneration diseases or brain function disorders by increasing the expression level of a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, which comprises using a polynucleotide comprising a polynucleotide encoding the G protein-coupled receptor protein or a partial peptide thereof.

26. A kit for screening a compound or its salt preventing and treating nerve degeneration diseases or brain function disorders by increasing the expression level of a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, which comprises a polynucleotide comprising a polynucleotide encoding the G protein-coupled receptor protein or a partial peptide thereof.

27. A compound or its salt preventing and treating nerve degeneration diseases or brain function disorders by increasing the expression level of a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1 or a partial peptide thereof, which is obtainable using the screening method according to claim 25 or the screening kit according to claim 26.

28. A prophylactic/therapeutic agent for nerve degeneration diseases or brain function disorders, which comprises a compound or its salt increasing the expression level of a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, or a partial peptide thereof.

29. The prophylactic/therapeutic agent according to claim 28, wherein the prophylactic/therapeutic agent is an agent for Alzheimer's disease, Parkinson's disease,

Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral disease, epidural hematoma or subdural hematoma.

30. A method of screening a compound or its salt inhibiting apotosis by increasing the expression level of a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, which comprises using a polynucleotide comprising a polynucleotide encoding the G protein-coupled receptor protein or a partial peptide thereof.

31. A kit for screening a compound or its salt inhibiting apotosis by increasing the expression level of a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, which comprises a polynucleotide comprising a polynucleotide encoding the G protein-coupled receptor protein or a partial peptide thereof.

32. A compound or its salt inhibiting apotosis by increasing the expression level of a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or a partial peptide thereof, which is obtainable using the screening method according to claim 30 or the screening kit according to claim 31.

33. An apotosis inhibitor comprising a compound or its salt increasing the expression level of a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or a partial peptide thereof.

34. A method of screening an agonist or antagonist to a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or to a salt thereof, which comprises using a compound or its salt that alters the binding property or signal transduction between (1) the G protein-coupled receptor protein, a partial peptide or a salt thereof and (2) humanin or a salt thereof.

35. A method of screening an agonist to a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10 or SEQ ID NO: 12 or to a salt thereof, which comprises measuring an inhibitory activity on intracellular cAMP formation upon bringing a test compound into contact with cells containing the receptor protein.

36. A method (i) for prevention/treatment of nerve degeneration diseases or brain function disorders, a method (ii) for prevention/treatment of Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral disease, epidural hematoma or subdural hematoma, or a method (iii) for inhibiting apotosis,

which comprises administering into a mammal an effective amount of (1) a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, or a partial peptide thereof or a salt thereof, (2) a polynucleotide comprising a polynucleotide encoding a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or a partial peptide thereof, or (3) an agonist to a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or to a salt thereof.

37. Use of (1) a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14, or a partial peptide thereof or a salt thereof, (2) a polynucleotide comprising a polynucleotide encoding a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 or a partial peptide thereof, or (3) an agonist to a G protein-coupled receptor protein comprising the same or substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO: 1, SEQ ID NO: 10, SEQ ID NO: 12 or SEQ ID NO: 14 in order to produce (i) a prophylactic/therapeutic agent for

nerve degeneration diseases or brain function disorders, (ii) a prophylactic/therapeutic agent for Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral diseases, epidural hematoma or subdural hematoma, or (iii) an apotosis inhibitor.

38. Humanin having an N-terminal methionine residue amino group of which is formylated, or a salt thereof.

39. The humanin according to claim 38 or its salt, which is a polypeptide or its salt, consisting of the amino acid sequence having an N-terminal methionine residue amino group of which is formylated, which is represented by SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8 or SEQ ID NO: 9.

40. A polypeptide or its salt consisting of the amino acid sequence represented by SEQ ID NO: 6 or SEQ ID NO: 9.

41. A pharmaceutical preparation comprising the humanin or its salt according to claim 38 or the polypeptide or its salt according to claim 40.

42. The pharmaceutical preparation according to claim 41, which is a prophylactic/therapeutic agent for nerve degeneration diseases or brain function disorders.

43. The pharmaceutical preparation according to claim 41, which is a prophylactic/therapeutic agent for Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral disease, epidural hematoma or subdural hematoma.

44. The pharmaceutical preparation according to claim 41, wherein the pharmaceutical preparation is an apotosis inhibitor.

45. A method (i) for prevention/treatment of nerve degeneration diseases or brain function disorders, a method (ii) for prevention/treatment of Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral

disease, epidural hematoma or subdural hematoma, or a method (iii) for inhibiting apotosis,

which comprises administering into a mammal an effective amount of the humanin or its salt according to claim 38 or the polypeptide or its salt according to claim 10.

46. Use of the humanin or its salt according to claim 38 or the polypeptide or its salt according to claim 40 in order to produce (i) a prophylactic/therapeutic agent for nerve degeneration diseases or brain function disorders, (ii) a prophylactic/therapeutic agent for Alzheimer's disease, Parkinson's disease, Down's syndrome, amyotrophic lateral sclerosis, prion disease, Creutzfeldt-Jakob disease, Huntington's disease, diabetic neuropathy, multiple sclerosis, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage, ischemic cerebral diseases, epidural hematoma or subdural hematoma, or (iii) an apotosis inhibitor.